

Network Meta-Analysis of the Efficacy of Acupuncture, Alpha-blockers and Antibiotics on Chronic Prostatitis/Chronic Pelvic Pain Syndrome

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Supplementary legends:

Supplemental Digital Content, including three tables (supplementary table 1, 2 and 3), and four figures (supplementary figure 1, 2, 3 and 4).

Supplementary Table 1 that summarizes mean, standard difference, and sample size between treatment groups for included studies in a network meta-analysis.

Supplementary Table 2 that represents the PRISMA-NMA checklist.

Supplementary Table 3 that describes the search strategy.

Supplementary Figure 1 that shows inconsistency test of NIH-CPSI total score.

Supplementary Figure 2 that shows inconsistency test of NIH-CPSI pain score.

Supplementary Figure 3 that shows inconsistency test of NIH-CPSI voiding score.

Supplementary Figure 4 that shows inconsistency test of NIH-CPSI QoL score.

Supplementary Table 1 NIH-CPSI Outcomes of Randomized Controlled Trials

Study	Treatment	Total score		Pain		Voiding		QoL		N
		mean	sd	mean	sd	mean	sd	mean	sd	
Nickel²¹	placebo	-6.5	8.5	-3	6.59	-1	3.65	-1.2	2	134
	α -blocker	-7.1	9	-3.3	6.6	-1.2	3.55	-1.2	2.17	138
Tugcu²²	placebo	-1	1.2	-0.6	0.85	-0.2	0.91	-0.2	1.1	29
	α -blocker	-12.4	1.61	-5.2	1.44	-3	0.91	-4.2	1	29
	dual therapy	-12.7	1.32	-5.4	1.21	-3.5	1.21	-3.8	0.9	28
Alexander²³	placebo	-3.4	5	-1.6	2.9	-0.5	2	-1.2	1.5	45
	α -blocker	-4.4	6.3	-2.3	3.7	-0.9	2	-1.3	2	45
	antibiotic	-6.2	7.3	-3	4.6	-1.3	2.1	-1.9	2.4	42
	dual therapy	-4.1	6.1	-1.8	3.7	-1.1	1.8	-1.3	1.9	49
Cheah²⁴	placebo	-10.2	10.6	-4.8	5.81	-1.8	3.65	-3.4	2	43
	α -blocker	-14.3	8.22	-6.5	4.96	-3.1	3.34	-4.7	3.07	43
Nickel²⁵	placebo	-2.9	8.31	-1.8	4.28	-0.2	2.85	-0.7	1.51	35
	antibiotic	-5.4	8.58	-1.7	4.85	-1.2	3	-1	1.7	45
Lee²⁰	acupuncture	-10.3	7.7	-4.3	3.3	-4.1	3.3	-5.8	4.9	44
	sham acupuncture	-5.9	7.7	-3.5	4.2	-2.3	3.5	-1.5	3.3	45
Lee²⁷	electro-acupuncture	-9.5	3.7	-5.2	1.9	-1.8	1.5	-2.6	2.4	12
	sham acupuncture	-3.5	3.6	-1.6	1.8	-0.7	1.4	-1.3	1.8	12
Sahin¹²	acupuncture	-15.9	3	-7.1	2	-2.4	1.1	-6.6	1.3	45
	sham acupuncture	-9.4	5.8	-4.8	1.9	-1	1.3	-4.3	2.4	46
Kucuk¹³	dual therapy	-6.4	5	-3.9	3	-0.8	1.4	-4.3	2.7	28
	electro-acupuncture	-12.5	6	-6.7	3.7	-1.8	2.5	-5.5	2.4	26
Zhou²⁶	placebo	-3.3	2.1	-1.5	2.1	-0.7	0.62	-1	1.32	24
	antibiotic	-17.2	2.43	-8.9	1.8	-4.7	0.69	-4.5	1.31	24
Nickel²⁸	placebo	-8.5	7.2	-4	3.6	-1.3	3	-2.7	2.5	51
	α -blocker	-12.1	9.3	-5.9	4.5	-2.2	2.7	-4.1	3.1	52
Chen²⁹	placebo	-4	2.3	-1.7	1.3	-1.1	0.7	-1.2	0.8	47
	α -blocker	-7.5	1.9	-4.4	1.3	-2	1.1	-1.3	1	46

Supplemental Table 2 PRISMA-NMA Checklist

Section/Topic	Item #	Checklist Item	Reported on Page #
TITLE			
Title	1	Identify the report as a systematic review <i>incorporating a network meta-analysis (or related form of meta-analysis).</i>	1
ABSTRACT			
Structured summary	2	Provide a structured summary including, as applicable: Background: main objectives Methods: data sources; study eligibility criteria, participants, and interventions; study appraisal; and <i>synthesis methods, such as network meta-analysis.</i> Results: number of studies and participants identified; summary estimates with corresponding confidence/credible intervals; <i>treatment rankings may also be discussed. Authors may choose to summarize pairwise comparisons against a chosen treatment included in their analyses for brevity.</i> Discussion/Conclusions: limitations; conclusions and implications of findings. Other: primary source of funding; systematic review registration number with registry name.	2
INTRODUCTION			
Rationale	3	Describe the rationale for the review in the context of what is already known, <i>including mention of why a network meta-analysis has been conducted.</i>	3
Objectives	4	Provide an explicit statement of questions being addressed, with reference to participants, interventions, comparisons, outcomes, and study design (PICOS).	4
METHODS			
Protocol and registration	5	Indicate whether a review protocol exists and if and where it can be accessed (e.g., Web	N/A

		address); and, if available, provide registration information, including registration number.	
Eligibility criteria	6	Specify study characteristics (e.g., PICOS, length of follow-up) and report characteristics (e.g., years considered, language, publication status) used as criteria for eligibility, giving rationale. <i>Clearly describe eligible treatments included in the treatment network, and note whether any have been clustered or merged into the same node (with justification).</i>	14
Information sources	7	Describe all information sources (e.g., databases with dates of coverage, contact with study authors to identify additional studies) in the search and date last searched.	14-15
Search	8	Present full electronic search strategy for at least one database, including any limits used, such that it could be repeated.	14-15
Study selection	9	State the process for selecting studies (i.e., screening, eligibility, included in systematic review, and, if applicable, included in the meta-analysis).	13-14
Data collection process	10	Describe method of data extraction from reports (e.g., piloted forms, independently, in duplicate) and any processes for obtaining and confirming data from investigators.	15
Data items	11	List and define all variables for which data were sought (e.g., PICOS, funding sources) and any assumptions and simplifications made.	15
Geometry of the network	S1	Describe methods used to explore the geometry of the treatment network under study and potential biases related to it. This should include how the evidence base has been graphically summarized for presentation, and what characteristics were compiled and used to describe the evidence base to readers.	16
Risk of bias within individual studies	12	Describe methods used for assessing risk of bias of individual studies (including specification of whether this was done at the study or outcome level), and how this information is to be used in any data synthesis.	15

Summary measures	13	State the principal summary measures (e.g., risk ratio, difference in means). <i>Also describe the use of additional summary measures assessed, such as treatment rankings and surface under the cumulative ranking curve (SUCRA) values, as well as modified approaches used to present summary findings from meta-analyses.</i>	16
Planned methods of analysis	14	Describe the methods of handling data and combining results of studies for each network meta-analysis. This should include, but not be limited to: <ul style="list-style-type: none"> • <i>Handling of multi-arm trials;</i> • <i>Selection of variance structure;</i> • <i>Selection of prior distributions in Bayesian analyses; and</i> • <i>Assessment of model fit.</i> 	16
Assessment of Inconsistency	S2	Describe the statistical methods used to evaluate the agreement of direct and indirect evidence in the treatment network(s) studied. Describe efforts taken to address its presence when found.	16
Risk of bias across studies	15	Specify any assessment of risk of bias that may affect the cumulative evidence (e.g., publication bias, selective reporting within studies).	15
Additional analyses	16	Describe methods of additional analyses if done, indicating which were pre-specified. This may include, but not be limited to, the following: <ul style="list-style-type: none"> • Sensitivity or subgroup analyses; • Meta-regression analyses; • <i>Alternative formulations of the treatment network; and</i> • <i>Use of alternative prior distributions for Bayesian analyses (if applicable).</i> 	16
RESULTS†			
Study selection	17	Give numbers of studies screened, assessed	14-15 ,

		for eligibility, and included in the review, with reasons for exclusions at each stage, ideally with a flow diagram.	Figure 1
Presentation of network structure	S3	Provide a network graph of the included studies to enable visualization of the geometry of the treatment network.	Figure 2
Summary of network geometry	S4	Provide a brief overview of characteristics of the treatment network. This may include commentary on the abundance of trials and randomized patients for the different interventions and pairwise comparisons in the network, gaps of evidence in the treatment network, and potential biases reflected by the network structure.	7, Table 1
Study characteristics	18	For each study, present characteristics for which data were extracted (e.g., study size, PICOS, follow-up period) and provide the citations.	Table 1
Risk of bias within studies	19	Present data on risk of bias of each study and, if available, any outcome level assessment.	Table 2
Results of individual studies	20	For all outcomes considered (benefits or harms), present, for each study: 1) simple summary data for each intervention group, and 2) effect estimates and confidence intervals. <i>Modified approaches may be needed to deal with information from larger networks.</i>	Supplementary Table 1
Synthesis of results	21	Present results of each meta-analysis done, including confidence/credible intervals. <i>In larger networks, authors may focus on comparisons versus a particular comparator (e.g. placebo or standard care), with full findings presented in an appendix. League tables and forest plots may be considered to summarize pairwise comparisons.</i> If additional summary measures were explored (such as treatment rankings), these should also be presented.	5-8
Exploration for inconsistency	S5	Describe results from investigations of inconsistency. This may include such information as measures of model fit to compare consistency and inconsistency models, <i>P</i> values from statistical tests, or summary of inconsistency estimates from	9

		different parts of the treatment network.	
Risk of bias across studies	22	Present results of any assessment of risk of bias across studies for the evidence base being studied.	5, Table 2
Results of additional analyses	23	Give results of additional analyses, if done (e.g., sensitivity or subgroup analyses, meta-regression analyses, <i>alternative network geometries studied</i> , <i>alternative choice of prior distributions for Bayesian analyses</i> , and so forth).	9
DISCUSSION			
Summary of evidence	24	Summarize the main findings, including the strength of evidence for each main outcome; consider their relevance to key groups (e.g., healthcare providers, users, and policy-makers).	9-11
Limitations	25	Discuss limitations at study and outcome level (e.g., risk of bias), and at review level (e.g., incomplete retrieval of identified research, reporting bias). <i>Comment on the validity of the assumptions, such as transitivity and consistency. Comment on any concerns regarding network geometry (e.g., avoidance of certain comparisons).</i>	12
Conclusions	26	Provide a general interpretation of the results in the context of other evidence, and implications for future research.	13
FUNDING			
Funding	27	Describe sources of funding for the systematic review and other support (e.g., supply of data); role of funders for the systematic review. This should also include information regarding whether funding has been received from manufacturers of treatments in the network and/or whether some of the authors are content experts with professional conflicts of interest that could affect use of treatments in the network.	18

Supplementary Table 3 Search Strategies

PubMed:

- #1 "chronic prostatitis"[Title/Abstract]
- #2 "chronic pelvic pain syndrome"[Title/Abstract]
- #3 "nonbacterial prostatitis"[Title/Abstract]
- #4 "chronic prostatitis/chronic pelvic pain syndrome"[Title/Abstract]
- #5 "chronic prostatitis-chronic pelvic pain syndrome"[Title/Abstract]
- #6 "CP/CPPS"[Title/Abstract]
- #7 "CP-CPPS"[Title/Abstract]
- #8 #1 OR #2 OR #3 OR #4 OR #5 OR #6 OR #7
- #9 "acupuncture"[MeSH Terms]
- #10 "acupuncture therapy"[MeSH Terms]
- #11 "acupuncture points"[MeSH Terms]
- #12 "auriculotherapy"[MeSH Terms]
- #13 "acupuncture"[Title/Abstract]
- #14 "acupoint"[Title/Abstract]
- #15 "auriculotherapy"[Title/Abstract]
- #16 OR/1-15
- #17 "adrenergic alpha-antagonists"[Pharmacological Action]
- #18 "adrenergic alpha-antagonists"[MeSH Terms]
- #19 adrenergic alpha receptor blockader*[Title/Abstract]
- #20 alpha blocke*[Title/Abstract]
- #21 "adrenergic alpha antagonists"[Title/Abstract]
- #22 "adrenergic alpha receptor blockader"[Title/Abstract]
- #23 alpha adrenergic blocker*[Title/Abstract]
- #24 "anti-bacterial agents"[MeSH Terms]
- #25 "anti-bacterial agents"[Pharmacological Action]
- #26 antibiotic*[Title/Abstract]
- #27 bactericide*[Title/Abstract]
- #28 antibacterial agent*[Title/Abstract]
- #29 #17 OR #18 OR #19 OR #20 OR #21 OR #22 OR #23 OR #24 OR #25 OR #26 OR #27 OR #28

#30 "Randomized Controlled Trial" [Publication Type]
#31 "Randomized Controlled Trials as Topic"[Mesh]
#32 "Pragmatic Clinical Trial" [Publication Type]
#33 "Pragmatic Clinical Trials as Topic"[Mesh]
#34 "Intention to Treat Analysis"[Mesh]
#35 "random allocation"[MeSH Terms]
#36 random*[Title/Abstract]
#37 #30 OR #31 OR #32 OR #33 OR #34 OR #35 OR #36
#38 #8 AND (#16 OR #29) AND #37

EMBASE:

#1 'chronic prostatitis'/exp
#2 'chronic prostatitis':ti,ab
#3 'chronic pelvic pain syndrome':ti,ab
#4 'nonbacterial prostatitis':ti,ab
#5 'chronic prostatitis/chronic pelvic pain syndrome':ti,ab
#6 'chronic prostatitis-chronic pelvic pain syndrome':ti,ab
#7 'CP/CPPS':ti,ab
#8 'CP-CPPS':ti,ab
#9 OR/1-8
#10 'acupuncture'/exp
#11 'acupuncture':ti,ab
#12 'acupoint':ti,ab
#13 'auriculotherapy':ti,ab
#14 OR/10-14
#15 'alpha adrenergic receptor blocking agent'/exp
#16 'adrenergic alpha antagonists':ti,ab
#17 'adrenergic alpha receptor blockader':ti,ab
#18 'alpha blocker':ti,ab
#19 'adrenergic alpha antagonists':ti,ab
#20 'adrenergic alpha receptor blockader':ti,ab
#21 'alpha adrenergic blocker':ti,ab
#22 'antiinfective agent'/exp

#23 anti bacterial agent*:ti,ab

#24 anti infective agent*:ti,ab

#25 antibiotic*:ti,ab

#26 bacteriocide*:ti,ab

#27 antibacterial agent*:ti,ab

#28 OR/15-27

#29 'randomized controlled trial'/exp

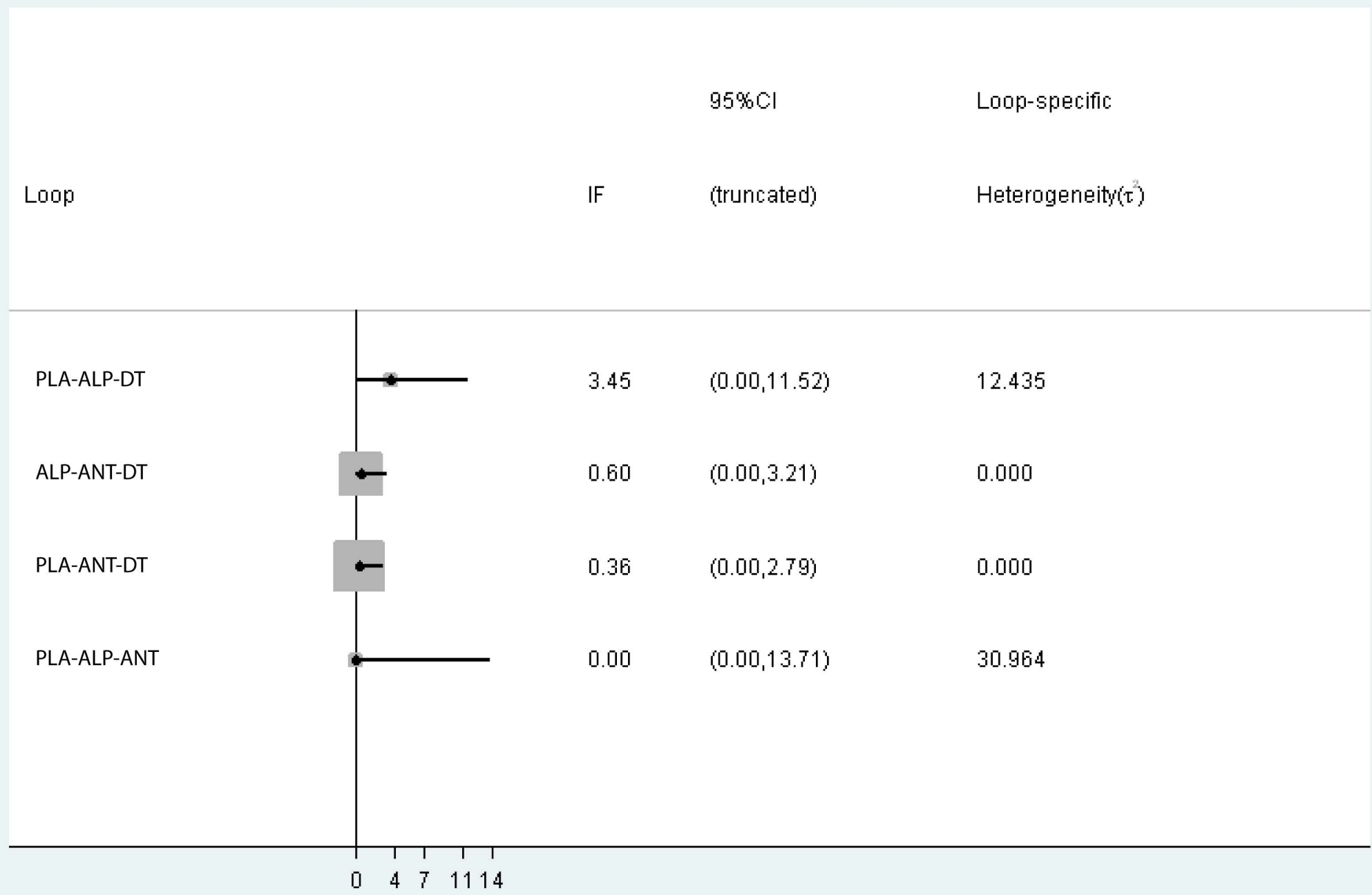
#30 'randomized controlled trial (topic)'/exp

#31 random*:ti,ab

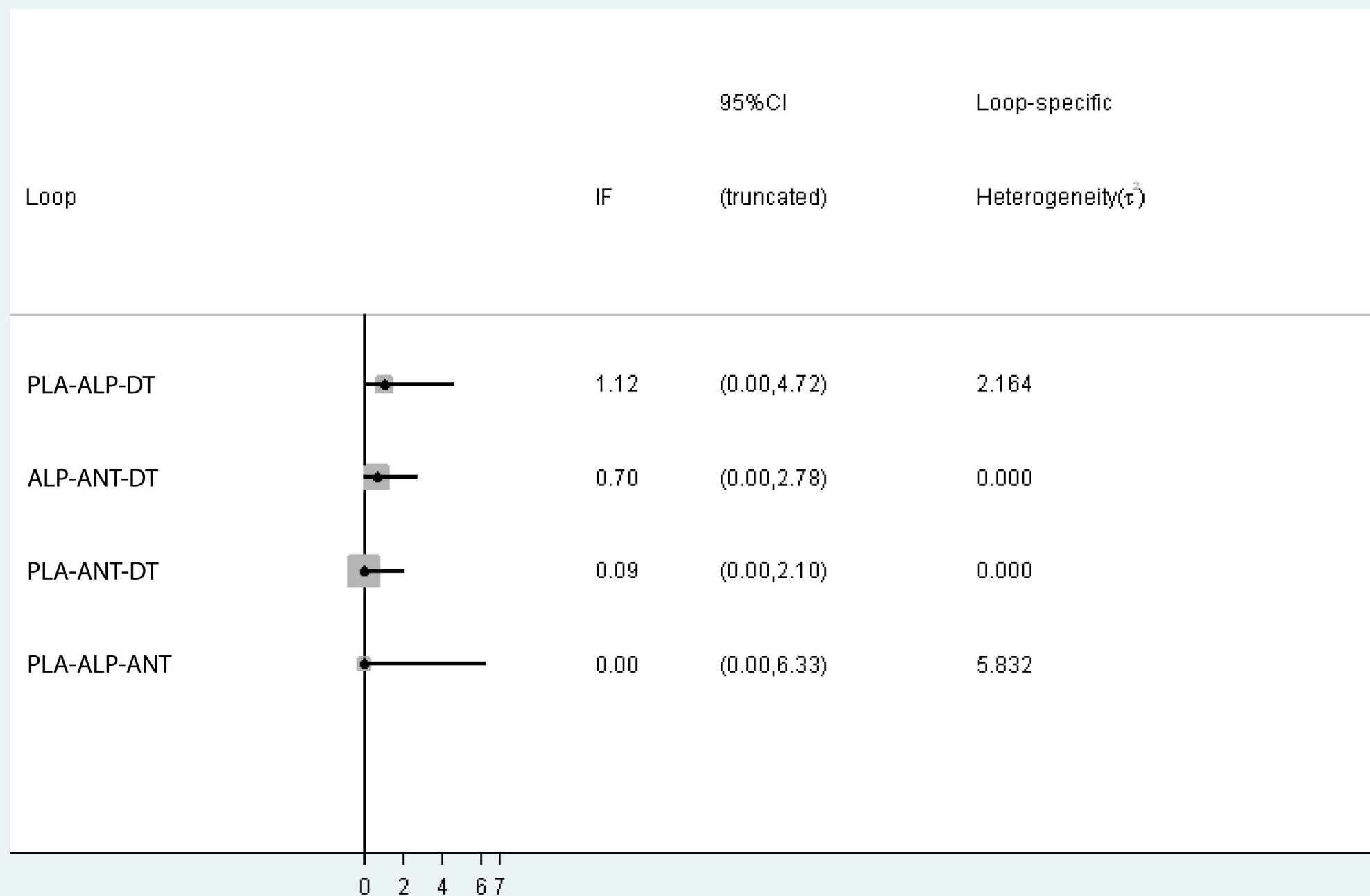
#32 OR/30-31

#33 #9 AND (#14 OR #28) AND #32

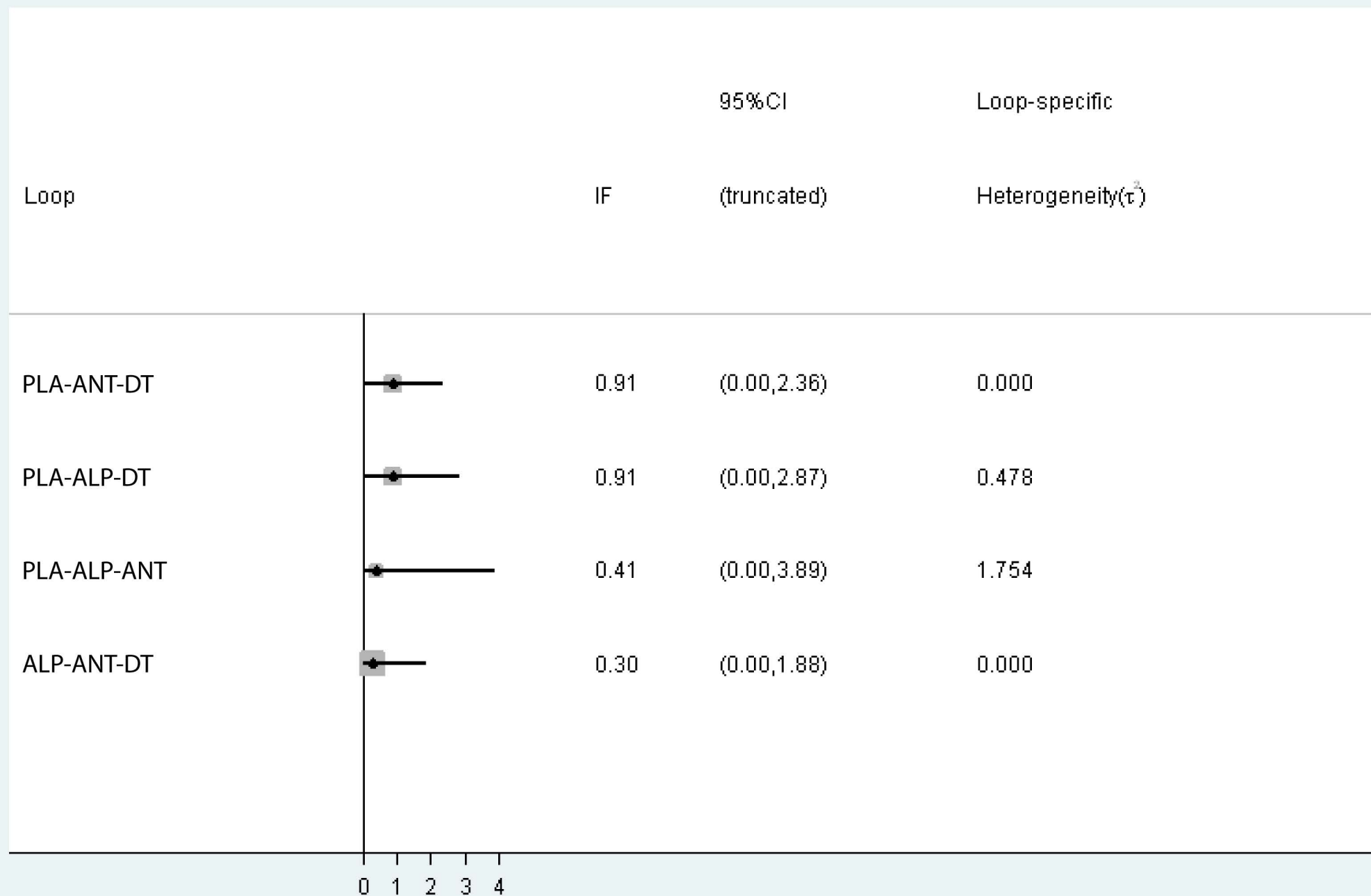
Supplementary Figure 1



Supplementary Figure 2



Supplementary Figure 3



Supplementary Figure 4

